REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 12-27, 31, 32 and 34-39 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 12-27, 29, and 31-37 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Ochoa et al. (U.S. Patent 5,443,983) in view of Rosenberg (U.S. Patent 4,690,915) and Melder et al. and further in view of the acknowledged prior art and Rooney et al., each further in view of Babbitt et al. (U.S. Patent 5,766,920) and Ochoa et al. (U.S. Patent 5,296,353). The examiner has combined the disclosures and teachings of the cited and applied references to take the position that the presently claimed invention is *prima facie* obvious on the assumption that the instant invention uses "autoiogous lymphocytes". This rejection is respectfully traversed.

A chart (Table 1) attached hereto provides a comparison between the specific disclosures of the cited and applied references, listed as references A-G, and the instant invention for disclosures of source of lymphocyte, stimulant, cytokine, subject disease, cell, and type of experiment. The concept of treating viral infections by first cultivating a lymphocyte from a virally infected patient (viremia) and then injecting it into

the virus-infected patient is unique to the instant invention. Such a concept is absent from Ochoa (ref. C in Table 1), in which a healthy twin's lymphocytes are cultivated with soluble anti-CD3 + IL2 and then injected into AIDS patients, resulting in no side effects but also with no confirmed anti-viral activity, or from references E-G (in Table 1), in which lymphocytes from healthy donors were used. Accordingly, the Ochoa reference (ref. C) and references E-G teach away from the presently claimed invention and it is clear that one of ordinary skill in the art undoubtedly would not be led to the present invention in view of the teachings away from the present invention in refs. C and E-G.

Other than the instant invention, the concept of cultivating lymphocytes from virally infected (viremia) patients first appeared in Shimizu et al., AIDS Research and Human Retrovirus 16:611 (2000), which reported that a large amount of HIV-free activated lymphocytes was obtained by cultivating an HIV patient's peripheral blood lymphocytes with anti-CD3 antibody in solid phase and IL-2. Before the Shimizu publication, which was published well after the present invention was made, there was no other report of the instant invention.

As for Ochoa, U.S. Patent 5,296,353 (ref. B in Table 1), Example 1 has confirmed the effect of reducing liver metastases of MCA-38 tumor by obtaining stimulant T cell that was cultivated from mouse lymphocytes and activated with anti-CD3

Ab + IL-2, injecting it into a tumor-bearing mouse, and then subsequently injecting IL-2 Liposome. It is, however, unclear whether this effect is due to activated T cell or to the subsequent injection of IL-2 Liposome, and it would be difficult to conclude that the effect is solely due to activated T cell. It is only the instant invention that has come to confirm for the first time the anti-viral activity by anti-CD3 stimulated T cell after cultivating virally infected patient's lymphocytes. All the examples, with the exception of Example 1, merely refer to *in vitro* cytotoxicity.

Rooney et al. and Wallace et al (reference F and G in Table 1) are directed to adoptive immunotherapy against viral infection using antigen-specific CTL, and it is clear that antigen-specific CTLs show anti-viral activity. In contrast, the instant invention is directed to adoptive immunotherapy using non-specifically activated T cells. As would be recognized by those of skill in the art, non-specifically activated T cell with anti-viral activity is distinct from virus-specific CTL with anti-viral activity.

It would certainly be clear that one of ordinary skill in the art would not be motivated to combine the disparate disclosures and teachings of the cited and applied references, some of whose teachings are directed away from the present invention, to arrive at the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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TABLE 1: COMPARISON WITH THE INSTANT INVENTION

Cited	Source of Lymphocyte	Stimulant	Cytokine	Subject Disease	Cell	Type of Experiment
A: Babbit USP 5,766,920	Autologous (human) (Not Viremia)	Soluble OKT3	IL-2	Cancer	CD3-T	*In vivo*
	Autologous (Chimp, Viremia?)	OKT3	Culture Supernatant	HBV (viral infection)	CD3-T	*In vivo*
B: Ochoa USP 5,296,353	Autologous (Mouse, Not Viremia)	Soluble anti-CD3 antibody	IL-2	Cancer	CD3-T	*In vivo* IL-2 Lipospme Five-day injection of
C: Ochoa USP 5,443,983	PBL, TIL (Allogenic, Not Viremia)	Soluble OKT3	IL-2	Cancer	CD3-T	*In vitro*
	Twin (Syngenic not Autologous, Not Viremia)	Soluble OKT3	IL-2	HIV viral infection	CD3-T	*In vivo* (toxicity not efficacy)
D: Rosenberg USP 4,690,915	Autologous (Not Viremia)	N/A	IL-2	Cancer	LAK	*In vivo*
E: Melder, *AIDS Res Hum Retrovirus* 6:1011 (1990)	HIV seronegative donor PBL (Allogenic, Not Viremia)	N/A	IL-2	HIV (viral infection)	A-LAK	*In vitro*
F: Rooney, *Lancet*, 345:9 (1995)	Donor PBL (Allogenic, Not Viremia)	EBV transformed B cell (antigen specific)	IL-2	EBV (viral infection)	CTL	*In vivo*
G: Wallace, *Eur J Immunol*, 12:1012 (1982)	Healthy donor (Allogenic, Not viremia)	EBV transformed B cell (antigen specific)	IL-2	EBV (viral infection)	CTL	*In vitro*
The instant invention	Autologous (viremia)	Immobilized OKT3	IL-2	EBV (viral infection)	CD3-T	*In vivo*